Urinary and hematologic indexes of hypohydration

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FRANCESCONI, R. P., R. W. HUBBARD, P. C. SZLYK, D. SCHNAKENBERG, D. CARLSON, N. LEVA, I. SILS, L. HUBBARD, V. PEASE, J. YOUNG, AND D. MOORE. *Urinary and hematologic indexes of hypohydration.* J. Appl. Physiol. 62(3): 1271–1276, 1987.—As part of a large-scale field feeding system test we were able to collect and study hundreds of aliquots of overnight urine samples obtained immediately prior to a fasting blood sample on *days 1, 20,* and *44* of the field test. The large number of experimental samples (>650) and concomitant collection of blood and urine aliquots along with data on body weights gave us the opportunity to assess and quantitate the sensitivity of commonly used criteria of hypohydration. Urine aliquots for all test days were initially categorized by specific gravity (SG) ≥ 1.03 ($n = 124$) or <1.03 ($n = 540$). Creatinine levels were elevated ($P < 0.001$) in the concentrated urine samples, but a decreased trend in sodium-to-potassium ratios in these samples failed to achieve statistical significance ($P > 0.05$). However, when individuals with high SG urine were subclassified by a criterion of weight loss >3% from original body weight, then creatinine concentrations were elevated ($P = 0.05$), whereas sodium-to-potassium ratios were decreased ($P = 0.05$) when subjects also with high SG but weight loss <3% were compared. Because of the moderate altitude (2,000 m) of the field site and the time of sojourn (44 days), there occurred a slight, but significant ($P < 0.001$), erythropoietic response. Hematocrit and serum osmolality were not significantly different when examined by the criteria of high or low SG urine and weight loss > or <3% original body weight. However, serum urea nitrogen-to-creatinine ratios were increased (*days 1* and *44*, $P < 0.05$) in test subjects whose urine samples exceeded 1.03 in SG. The results of this study indicated that mild hypohydration, manifested in concomitant elevations in urinary SG and creatinine, was not reflected in the common circulatory indexes of hypohydration, i.e., hematocrit and osmolality. Alternatively, urea nitrogen-to-creatinine ratio may be a sensitive circulatory index of imminent hypohydration.

specific gravity; creatinine; hematocrit; osmolality; urea nitrogen; sodium-to-potassium ratio

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TOTAL BODY WATER LEVELS (hydration status) are most accurately quantitated using very sophisticated and expensive stable-isotope methodology (22) that is not generally available. Over the years, however, several circulating and urinary indexes have been examined to determine their covariability with body weight (water) loss and the reliability of using these indexes as general markers of hypohydration (1, 14, 23, 26). In the current experiments the availability of large numbers of test subjects and experimental samples and the nearly simultaneous collection of overnight urine aliquots and fasting blood samples allowed us to examine quantitatively the sensitivity and accuracy of the commonly used indexes of hydration status and hypohydration intensity.

In most studies of acute hypohydration water deficits are effected during a prior interval of exercise in the heat until the targeted weight loss is achieved (4, 20, 21). Additionally, several investigators have withheld rehydration solutions during an experimental heat stress and measured body weight prior and subsequent to the experimental interval (18, 26) to assess hypohydration level. During these experimental scenarios serial blood samples have been analyzed for several combinations of hematocrit, hemoglobin, sodium, osmolality, and protein to document and quantitate several of the clinical indexes of hypohydration. Further, the intensity of hypohydration has been correlated not only with plasma indexes but also with an increased physiological cost of work in the heat (21) and an elevated response pattern of stress and fluid regulatory hormones (9). The comparative value of electrolyte replacement solutions has been assessed during several of these experimental protocols, and, generally, reports indicate that water is equally efficacious in replacing body fluids and reducing the physiological cost of work in the heat (4, 5, 10).

Alternatively, we are unaware of any longitudinal studies that have assessed and correlated urinary indexes of hypohydration with body weight changes or circulating indexes of hypohydration. Minard et al. (17) studied 1,500 men in a field setting and related the degree of hypohydration to reduced urinary volume and electrolytes and increased specific gravity. Strydom et al. (25) reported that during a 6.5-h 18-mile road march urine volume was reduced to an average of 134 ml while sweat losses increased to ~4.5 liters and the mean body weight loss was 2.9%. Leithead and Pallister (15) studied men undergoing heat acclimation in a field setting and reported that 24-h urine samples of <500 ml ordinarily manifested specific gravities (SG) >1.03. However, none of these studies attempted to correlate the degree of hypohydration with other urinary or circulating indexes.

In a recently completed, large-scale field test of newly developed rations, we collected and examined overnight urine aliquots obtained just prior to a fasting blood sample. The large number of test subjects (initially 230) and three sampling times (*days 1, 20, 44*) during the field scenario afforded us the opportunity to examine several circulating as well as urinary indexes of hypohydration. Close monitoring of body weight, simultaneous blood and urine samples, and large numbers of test subjects permitted us to evaluate the sensitivity of variables in both

urine and plasma or serum, which have been classified as indexes of hypohydration.

METHODS

Test subjects (n = 230) were adult male and female (17% of total) members of US Army units that were deploying to a field site as part of their routine annual training cycle. All test subjects were fully informed of the testing procedures and potential risks and signed an agreement of voluntary participation. Test subjects reserved the right to withdraw without retribution.

In garrison before deployment a base-line body weight was obtained while each test subject was clad in fatigue trousers, T shirt, boots, socks, and undergarments. All subsequent weights were taken identically and a correction factor (2.7 kg) was subtracted to closely approximate nude body weight. Remaining measurements were made in the field setting on the first (*T1*), 20th (*T20*), and 44th (*T44*) days of field deployment.

On the evening prior to an experimental day prelabeled urine containers were delivered to each test subject, and he or she was instructed to collect at least 25 ml of the first-void urine of the subsequent morning. Although total urine volumes would have been useful, the sheer number and size of the necessary containers would have been impractical for storage, transport, and disposal. Urine containers were then hand carried to investigators between 0500 and 0700 h. A small aliquot of the fresh urine was immediately assayed for specific gravity in a field laboratory by refractometry (10400A TS Meter, AO Reichert Scientific Instruments, Buffalo, NY). Further aliquots were prepared and deep frozen for analysis of creatinine, sodium, and potassium. These latter assays were performed at a hospital laboratory where the samples were air transported while frozen. Creatinine was quantitated on a Gilford Stasar IV semiautomated spectrophotometer by methods outlined in their technical bulletin (Gilford Diagnostics, Cleveland, OH). Sodium (Na^+) and potassium (K^+) were quantitated using an FLM 3 flame photometer (Radiometer, Copenhagen) also by generally described methods.

Blood was taken without stasis from a superficial arm vein by trained phlebotomists after test subjects remained in an upright posture for at least 20 min. This blood sample was taken ~0.5–2.0 h after the urine sample, consistently while the subject was in a fasted (overnight) state and at the same time of day (0500–0700 h). Vacutainers (10 ml, Becton-Dickinson, Rutherford, NJ), either without additives or pretreated with heparin, were used for this purpose, but blood samples were taken at the same time from a single venipuncture. The blood samples were either processed immediately for hematocrit determination (uncorrected for trapped plasma) or allowed to clot (no additive) for 30–45 min, after which the sample was centrifuged (2,000 g, 4°C, 30 min) and the serum layer was removed. Hematocrit was measured in the heparinized sample after centrifugation at ~12,000 g in a microhematocrit centrifuge (IEC model MB). Since female test subjects comprised a consistent percent of the total test subject population as well as a consistent percent of the total test subjects with SG ≥1.03, their hematocrit data were incorporated into a single mean with that of the male subjects. A small serum aliquot was assayed expeditiously at the field site for osmolality by freezing-point depression (μOsmette, Precision Systems, Natick, MA). The remaining serum was divided into aliquots, deep frozen, and air transported for the subsequent analysis of urea nitrogen (Gilford Stasar IV) and creatinine.

Appropriate group means were compared for statistical significance using Student's nonpaired t test for independent data (16). The null hypothesis was rejected at $P \leq 0.05$. A urinary SG ≥1.03 was used as an initial criterion of hypohydration, and this group was generally compared with the remainder of test subjects (and trials) manifesting a SG <1.03. Test subjects with a SG ≥1.03 were subdivided further into two groups for comparative purposes only: > or <3% body weight loss (from predeployment level) determined immediately prior to phlebotomy on each experimental day. Individuals with SG >1.03 and body weight losses >3% might be categorized as hypohydrated by these field-expedient criteria; close comparison and evaluation of these criteria with circulating indexes was accomplished. Because the field deployment was executed at an elevation of ~2,000 m, there occurred a slight, but consistent, hematopoietic response over the prolonged experimental interval. Consequently, circulatory variables are reported by test day.

RESULTS

Table 1 illustrates mean values of urinary variables when the calculations were based and separated initially on the criterion of specific gravity (left side) for all test days (*T1, T20*, and *T44*). The data indicate that of 664 samples taken on 3 days (*T1, T20*, and *T44*), 124 (18.7%) manifested SG ≥1.03 as an initial criterion of hypohydration. (It should be noted that the slight inconsistencies in the n reported for the variables in Table 1 were probably due to the loss of a sample between the remote field site and the hospital laboratory or failure to report a data point.) However, when this group (SG ≥1.03) was further subdivided and examined by weight loss (< or >3% of predeployment body wt), mean specific gravities were virtually identical (SG = 1.0318, $P > 0.05$) in the two groups. Using the same criteria, we observed that creatinine concentrations were analogously greatly increased ($P < 0.001$) in the concentrated urine samples (SG ≥1.03). Furthermore, when creatinine concentrations were compared by body weight criteria in all samples having SG ≥1.03, individuals losing <3% body weight had significantly ($P = 0.05$) reduced concentrations (<3% body wt loss, mean = 3.10 g/l and >3% body wt loss, mean = 3.41 g/l). Urinary Na^+/K^+ was not significantly different in dilute and concentrated urines (mean = 3.99 and 3.61, respectively, $P > 0.05$). However, it is noteworthy that when urines with SG ≥1.03 were examined by weight loss of the test subject, the Na^+/K^+ was significantly ($P = 0.05$) reduced in test subjects having a weight loss >3% of predeployment body weight.

Data for hematocrit and other circulatory variables are illustrated in Tables 2–4. (It should be noted that for Tables 2–4 the consistent decrements in total test sub-

TABLE 1. *Mean urinary specific gravity, creatinine, and sodium-to-potassium ratios*

	All Subjects-All Trials		Subjects with SG > 1.03	
	SG < 1.03	SG > 1.03	Wt loss < 3%	Wt loss > 3%
		Specific gravity		
n	540	124	93	31
Mean	1.0215	1.0318	1.0318	1.0318
SD	0.005	0.0017	0.002	0.0015
SE	0.0002	0.0002	0.0002	0.0003
t	22.629		0	
P	<0.001		>0.05	
		Creatinine, g/l		
n	540	124	93	31
Mean	1.88	3.19	3.10	3.41
SD	0.73	0.67	0.75	0.55
SE	0.03	0.06	0.078	0.099
t	18.30		2.12	
P	<0.001		0.05	
		Na^+/K^+		
n	539	122	92	30
Mean	3.99	3.61	3.78	2.985
SD	2.23	1.82	1.91	1.26
SE	0.10	0.16	0.2	0.23
t	1.75		2.16	
P	>0.05		0.05	

Columns on left compare values in subjects having specific gravities (SG) > and < 1.03; those on right compare values only in subjects having SG > 1.03 and further classified by weight loss.

jects represented test subject attrition.) The slight hemoconcentration (Table 2) noted generally by test date regardless of other criteria was indicative of a slight erythropoietic response due to prolonged exposure (44 days) at the moderate altitude (2,000 m) (e.g., SG < 1.03, mean = 47.7 at *T1* and mean = 49.2 at *T44*, $t = 4.69$, $P < 0.001$). Interestingly, hematocrits were not significantly different on any of the test days when subjects were separated and compared by the urinary specific gravity criterion. Likewise, in test subjects with urinary SG ≥1.03, weight loss of > or <3% of body weight had no effect on hematocrit ($P > 0.05$).

Analogous results were noted for serum osmolality as illustrated in Table 3, although sojourn at the moderate altitude of this experiment apparently had no effects on serum osmolality under all criteria. Examination of values for serum osmolality on all test days indicated that test subjects having a urine SG ≥1.03 manifested no significant differences ($P > 0.05$) compared with subjects with SG <1.03. Likewise, no differences ($P > 0.05$) were observed in subjects with > or <3% body weight loss and SG >1.03.

The data in Table 4 demonstrated that prolonged altitude exposure had no effects on serum urea nitrogen-to-creatinine ratios (UN/Creat). However, on *T1* and *T44* subjects with urine SG ≥1.03 also had significantly ($P < 0.05$) elevated UN/Creat. On *T20*, while the trend was maintained, statistical significance was not achieved ($P > 0.05$). When test subjects with SG ≥1.03 were categorized in terms of body weight loss, no significant differences were noted in UN/Creat.

DISCUSSION

Increasing body water deficit or hypohydration has long been associated with an increased risk of heat illness (2, 14, 23). Thus it is not unexpected that during times when fluid consumption may be inadequate to meet thermoregulatory, metabolic, and cardiovascular requirements, homeostatic mechanisms are activated to conserve body fluids; one of the very early manifestations of this conservation is the production of a concentrated urine. For example, acute exposure to heat or exercise stress or fluid restriction usually elicits marked increases in circulating levels of hormones such as vasopressin (11, 12), angiotensin I (3, 6), and aldosterone (7, 8), all of which function to retain body fluids, increase urine concentration, and decrease urine volume. Thus it may be concluded that a urinary specific gravity of ≥1.03 is indicative of hypohydration, impending hypohydration or, if transient, may be simply reflective of a homeostatic adaptation to prevent debilitating hypohydration. Generally, the results of the present investigation indicate that in the vast majority of cases a concentrated urine sample did not reflect frank hypohydration, since two of the generally accepted criteria of hypohydration, hematocrit (18, 26) and osmolality (1, 5), were unaffected when test populations were categorized by urinary specific gravity. Thus those test subjects with SG ≥1.03 were probably very mildly hypohydrated or, more likely, actively concentrating urine to prevent hypohydration.

In a controlled laboratory setting wherein a heat-

TABLE 2. *Mean hematocrit levels on each test day*

	Hematocrit			
	All subjects		Subjects with SG > 1.03	
	SG < 1.03	SG > 1.03	Wt loss < 3%	Wt loss > 3%
		T1		
n	186	49	46	3
Mean	47.7	48.1	48.1	47.8
SD	3.18	2.2	2.1	4.01
SE	0.23	0.31	0.31	2.31
t	0.83			
P	>0.05			
		T20		
n	176	43	28	15
Mean	48.3	48.3	48.3	48.35
SD	2.66	2.39	2.08	2.97
SE	0.20	0.36	0.39	0.77
t	0		0.06	
P	>0.05		>0.05	
		T44		
n	171	32	19	13
Mean	49.2	49.8	49.4	50.3
SD	3.03	2.73	2.71	2.78
SE	0.23	0.48	0.62	0.77
t	1.04		0.91	
P	>0.05		>0.05	

Columns on left denote values in subjects having urinary specific gravities (SG) > and < 1.03; those on right compare values only in subjects having SG > 1.03 and further classified by weight loss. *T1*, *T20*, and *T44*, test days.

TABLE 3. *Mean serum osmolality on each test day*

	Serum Osmolality, mosmol/kg					
	All subjects			Subjects with SG > 1.03		
	SG < 1.03		SG > 1.03	Wt loss < 3%		Wt loss > 3%
			T1			
n	186		48	45		3
Mean	290.8		291.3	291.6		287.3
SD	6.05		5.48	5.39		6.43
SE	0.44		0.79	0.80		3.71
t		0.52				
P		>0.05				
			T20			
n	177		43	28		15
Mean	289.2		289.6	289.8		289.2
SD	4.07		4.05	3.48		5.06
SE	0.31		0.62	0.66		1.31
t		0.58			0.46	
P		>0.05			>0.05	
			T44			
n	171		32	19		13
Mean	288.9		290.4	290.2		290.8
SD	4.27		3.22	3.5		2.9
SE	0.33		0.57	0.8		0.8
t		1.89			0.51	
P		>0.05			>0.05	

Columns on left denote values in subjects having urinary specific gravities (SG) > and < 1.03; those on right compare values only in subjects having SG > 1.03 and further classified by weight loss. *T1*, *T20* and *T44*, test days.

exercise regimen without rehydration and with frequent assessment of body weight is employed to induce hypohydration, water loss and sweat rate can be closely monitored and percent body weight loss may be an accurate reflection of hypohydration level. In the present long-term field experiment body weight may provide a general indication of hydrational status, but, clearly, caloric consumption will also affect this variable over a 44-day period. In fact, mean caloric consumption on the day prior to sample collection was ~2,100 kcal among individuals with SG >1.03 and body weight loss >3% (mean wt of this population = 79.4 kg). If this group required ~3,000 kcal/day to maintain caloric equilibrium, then a caloric decrement may have contributed to the net weight loss over the experimental interval.

This may be related to the observation that mean urinary specific gravity was identical when individuals with high specific gravity were subclassified by weight losses either > or <3% of predeployment body weight, whereas urinary creatinine concentration was significantly increased in individuals with the greater weight loss. It is possible that this increment in the higher weight loss subjects may be associated with a slight reduction in muscle mass, which could give rise to an elevated urinary creatinine content. Of course, the greatly increased urinary creatinine in samples having high specific gravity was as expected in these concentrated samples.

However, a decreased urinary Na^+/K^+ was also anticipated in high specific gravity urine specimens (4, 17), since the aforementioned endocrinological adaptations would potentially promote sodium conservation and potassium excretion. The actual data indicate that the logical trend was apparent, but statistical significance was not achieved. However, when individuals with high specific gravity urine were examined by weight loss, individuals with the greater weight loss did manifest a significantly depressed Na^+/K^+. This could be reflective of increased reabsorption and decreased excretion of sodium in this subgroup or increased potassium excretion related to the aforementioned speculation on muscle mass. Since circulating indexes of hypohydration were not markedly different when these were compared for individuals with high and low specific gravity urine, it is difficult to attribute the differing urinary creatinine concentrations and Na^+/K^+ to variable intensities of hypohydration. This conclusion is strengthened by the observation that when the high specific gravities were compared by the body weight loss criterion, mean specific gravities were virtually identical. These observations are consonant with the hypothesis that plasma volume is defended to maintain cardiovascular stability, and plasma indexes are unaffected until a threshold level of total body water loss has been achieved.

As noted earlier, hematologic criteria were considered by experimental day, since prolonged, though moderate, altitude exposure may induce an erythropoietic response

TABLE 4. *Mean serum urea nitrogen-to-creatinine ratios on each test day*

	Serum Urea Nitrogen/Creatinine					
	All subjects			Subjects with SG > 1.03		
	SG < 1.03		SG > 1.03	Wt loss < 3%		Wt loss > 3%
			T1			
n	185		49	46		3
Mean	13.6		14.9	14.7		18.2
SD	3.07		3.96	3.91		3.95
SE	0.22		0.57	0.58		2.28
t		2.47				
P		0.02				
			T20			
n	178		42	27		15
Mean	13.4		14.5	14.4		14.7
SD	3.52		2.93	3.04		2.82
SE	0.26		0.45	0.58		0.73
t		1.88			0.31	
P		>0.05			>0.05	
			T44			
n	171		32	19		13
Mean	13.3		14.9	14.7		15.1
SD	3.23		3.25	2.72		4.0
SE	0.25		0.57	0.62		1.11
t		2.57			0.34	
P		0.02			>0.05	

Columns on left denote values in subjects having urinary specific gravities (SG) > and < 1.03; those on right compare values only in subjects with SG > 1.03 and further classified by weight loss. *T1*, *T20*, and *T44*, test days.

(24). Grover et al. (13) have recently reviewed data indicating that acute changes in hematocrit during the first several days exposure to 3,800 m are probably related to a reduction in plasma volume, whereas over several weeks an erythropoietic response will occur. Thus, in the current experiments the increased hematocrits at *T20* and *T44* may be a reflection of slightly increased erythrocyte production at this moderate altitude. Comparison of hematocrits in subjects having urine specific gravities <1.03 on *T1* vs. *T44* demonstrated small (3.14%), but highly significant ($P < 0.001$), increments in hematocrit. However, comparison of hematocrits by the criterion of urinary specific gravity or specific gravity and body weight loss indicated that the frequency of concentrated urines did not correlate with hemoconcentration. Again, we interpret this as an adaptive response among a large group of young healthy test subjects to prevent circulatory hypohydration during an interval of marginally adequate fluid intake (~3.5-4 l/day from all sources) despite moderate environmental conditions (20-25°C wet-bulb globe temperature).

Analogous results were noted for serum osmolality in terms of the specific gravity and body weight loss criteria. Unlike hematocrit, however, there occurred no effect of altitude on this variable. Serum osmolalities were remarkably consistent on each test day between specific gravity or weight loss groups; this consistency did not change when all test days were considered collectively. In fact, of the hematologic variables examined only serum UN/Creat provided statistically significant data when analyzed subsequent to specific gravity categorization.

In the absence of kidney malfunction the reabsorption of urea is closely associated with the reabsorption of water (19). Thus, when urine volume is reduced, urea reabsorption is increased. Since creatinine clearance is independent of urine volume, circulating UN/Creat has been utilized as a clinical index of hypohydration. In individuals with urine SG ≥1.03 this variable was a more sensitive index of prodromal hypohydration than either hematocrit or osmolality, since at *T1* and *T44* this ratio was significantly increased and at *T20* the same trend was evident in the absence of statistical significance.

We have concluded from these data that occurrence of highly concentrated urine specimens, determined by marked elevations in specific gravity and creatinine concentrations, did not indicate concomitant increases in hematocrit or plasma osmolality. Further, when body weight loss >3% was combined as a criterion with high specific gravity, then urinary creatinine levels were increased and Na^+/K^+ values were attenuated when subjects losing <3% of body weight were compared. Likewise, when mean hematocrit and serum osmolality were separated and compared by the criterion of urinary specific gravity for all 3 blood-sampling days, increased specific gravity could not be correlated with either hematocrit or osmolality. This may imply that the elevated specific gravity was indicative of a very moderate hypohydration not of sufficient intensity to induce alterations in hematocrit or osmolality. Alternatively, the significant alterations in UN/Creat may likewise imply that this is a more sensitive criterion of very moderate or prodromal hypohydration. It should not be concluded that urinary specific gravity should be discounted as a field-expedient technique for detecting hypohydration or impending hypohydration. Several points are relevant: consecutive urine samples with SG >1.03 may be clinically more evaluative; the value of SG >1.03 may be important (even in our elevated samples the mean SG was only 1.0318); logistically, SG can be assessed noninvasively and under all field conditions in a matter of seconds, whereas many of the other variables assessed in this study require more sophisticated techniques and equipment. Further studies are planned utilizing stable-isotope technology to quantitate hypohydration and to compare body water deficits with urinary and circulating indexes.

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